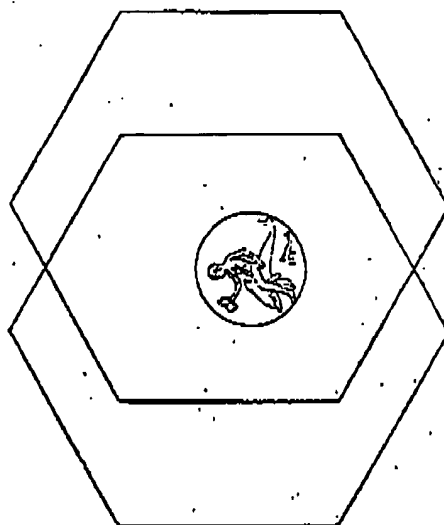


# TEXTBOOK OF ORGANIC CHEMISTRY

LOUIS F. FIESER  
and MARY FIESER



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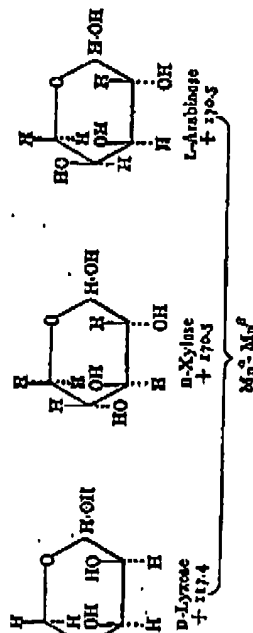
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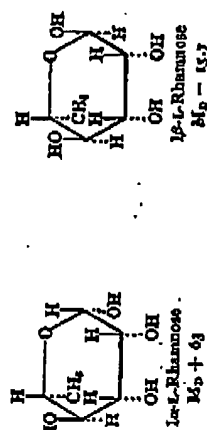
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rotations deviates from the average of +240 to the extent of only  $\pm 15$  (average).

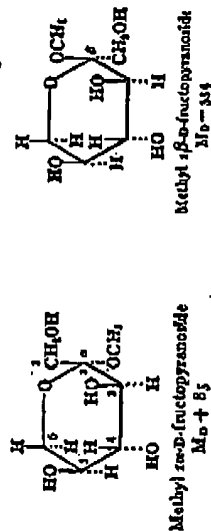
The data of Table I include a number of illustrations of the general relationship that in a pair of glycosidic epimers the isomer with the glycosidic hydroxyl or alkoxy group in the  $\alpha$ -orientation (down, to the rear) is invariably more dextrorotatory than the  $\beta$ -epimer. The rule holds for the pentoses, D-xylose, D-xylose, and L-arabinose, for the molecular rotation differences ( $\alpha - \beta$ ) are all positive:



The example of L-arabinose and the further example of L-rhamnose, a natural methylpentose, show that in the L-series, as in the D-series, the glycosidic carbon makes a greater dextrorotatory contribution when the



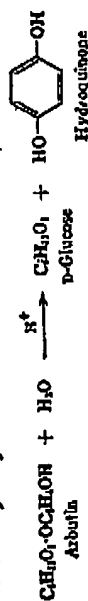
hydroxyl is oriented below the plane of the ring ( $\alpha$ ) than when above the plane ( $\beta$ ). D-fructose forms a pair of methylpyranosides epimeric at C<sub>2</sub>; the one with the glycosidic methoxyl oriented below the plane of the ring



is defined as the  $\alpha$ -isomer and, in conformity with the general rule, this isomer is the more dextrorotatory member of the pair.

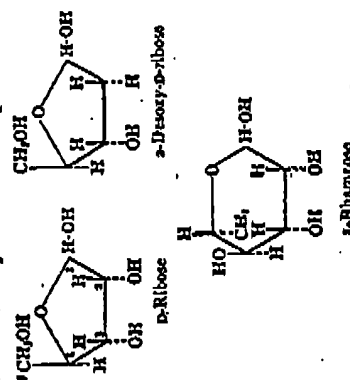
## GLYCOSIDES

The synthetic methylglycosides resulting from acid-catalyzed action of methanol on glucose exemplify a type of compound of abundant occurrence in plants. These are acetals, comparable to methylglucosides, and are derived from combination of various hydroxy compounds with various sugars. They are designated specifically as glucosides, mannosides, galactosides, etc., and the group as a whole is described by the generic name glycoside. When a sugar is combined with a nonsugar, the latter is described as an aglycone. The glycosides are also a sugar unit, the combination is a di-, tri-, or polysaccharide. The glycosides are hydrolyzed by mineral acids to the sugar and the aglycone; for instance arbutin, a glycoside obtained from the bearberry (*Arctostaphylos uva-ursi*), yields glucose and hydroquinone on hydrolysis:



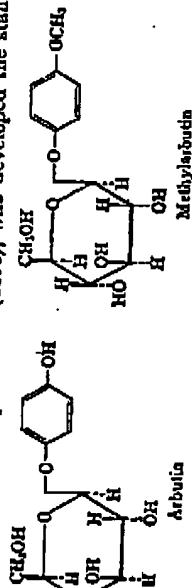
Usually an enzyme that can accomplish the hydrolysis occurs in the same plant, though in different cells. When the plant tissues are macerated the enzyme comes into contact with the glycoside and hydrolysis results. Although many enzymes can act on only one substance (substrate), others are not entirely specific in their activity. The widely distributed emulsin and maltase both hydrolyze many glycosides, but the differentiation first noted by Fischer, namely that the former acts on  $\beta$ -glucosides and the latter on  $\alpha$ -glucosides, is true for  $\alpha$ - and  $\beta$ -glycosides generally, and is frequently used as a proof of the type of glycoside linkage. The vast majority of natural glycosides possess the  $\beta$ -configuration.

Glucose is the most common sugar component, but several interesting sugars occur only as glycosides. The rare pentose D-those and its 2-deoxy derivative were first isolated by Levene from plant nucleic acids and thy-



monocyclic acids, respectively. Both sugars occur in the furanoside form shown in the formulas. L-Rhamnose, a methylpentose, is encountered in glycosides; its origin is puzzling since the configuration is that of L-mannose, which is unknown in nature, and hence it probably is not formed by simple reduction of the primary alcohol group of a hexose. Rhamnosides are hydrolyzed by a type-specific enzyme, rhamnase.

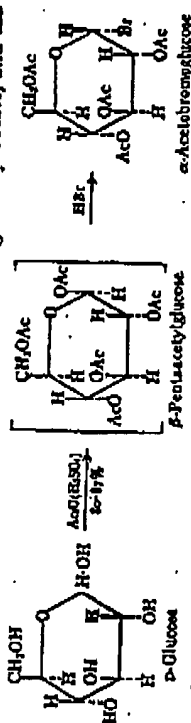
Arbutin and Methylarbutin. — These glucosides are hydrolyzed by emulsin to glucose and to hydroquinone and hydroquinone monomethyl ether, respectively, and hence are considered to be  $\beta$ -glucosides. Methylarbutin was synthesized by Michael (1881), who developed the standard



method for synthesis of glycosides. The glycosidic linkage is effected by condensing the aglycone with acetobromoglucose. Acetobromoglucose is

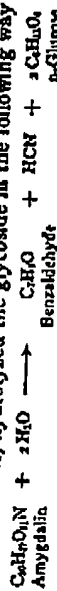


now considered to be an  $\alpha$ -derivative and is usually prepared by treating the pentacetate with hydrogen bromide in glacial acetic acid solution. In the condensation reaction a Walden inversion generally occurs, and the



product is a  $\beta$ -glycoside. Both glycosides can be obtained if the condensation is carried out in the presence of quinoline.

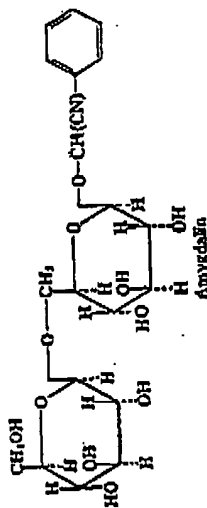
Amygdalin. — Amygdalin is the best known of the group of cyanophoric glycosides, so named because hydrogen cyanide is liberated on hydrolysis. Amygdalin was isolated in 1830 from seeds of the bitter almond (*Prunus amygdalus*) and soon attracted the attention of Liebig and Wöhler, who found that a proteinaceous substance emulsin, which could be extracted by water from the seeds, hydrolyzed the glycoside in the following way:



If a yeast extract is employed instead of emulsin, glucose and a glucoside of *d*-mandelonitrile that is identical with prunasin (*Prunus* species) are ob-



tained, which shows that hydrogen cyanide is part of the aglycone, and that the sugar unit is a disaccharide, identified in 1923 as the rare gentiobiose.



#### DISACCHARIDES

Disaccharides can be regarded as glycosides in which the aglycone is a second monosaccharide unit. They resemble monosaccharides in that they are very soluble in water and have a sweet taste. Only three occur as such in nature, sucrose (cane sugar), lactose (milk sugar), and maltose, and the latter is found free only occasionally. Disaccharides are encountered frequently as glycosides: gentiobiose from amygdalin is one example. Two disaccharides, maltose and cellobiose, are important because they are hydrolysis products of starch and cellulose, respectively.

Sucrose. — Sucrose on hydrolysis with acids or the enzyme invertase (plants, yeast, animals) yields D-glucose and D-fructose in equal amounts. Sucrose does not reduce Fehling's solution or form derivatives with phenylhydrazine, and hence the two sugar units are linked through the glycosidic hydroxyl group of each sugar and contain no free or potential carbonyl groups. Unlike the majority of sugars, sucrose crystallizes readily, probably because it does not undergo mutarotation in solution. The ring structure of the two component units was established (Haworth, 1916) by hydrolyzing completely methylated sucrose (see next page). One product was the usual tetramethyl- $\alpha$ -glucose, but the other was a tetramethylfructose derivative unknown at the time. Its structure was not established until ten years later, when it was found to contain a furanose, or 2,5-oxide ring. No combined fructose has ever been found to have the normal or pyranose structure. The glucose unit probably has the  $\alpha$ -configuration, since sucrose is hydrolyzed by maltase (an  $\alpha$ -glucosidase); the configuration of the fructose unit is not established, but is considered to be  $\beta$ . Recombination of the two units by purely chemical methods has not been achieved, but has been effected through the action of an enzyme on a mixture of glucose 1-phosphate and fructose (Hassid).

Sucrose has been used as an important foodstuff for centuries. Originally the only commercial source was the juice of sugar cane, a tropical